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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/560,803	04/28/2000	Won-Bin Young	P04014US1	5114

22885 7590 08/27/2003

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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	21

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/560,803	YOUNG ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-39* is/are pending in the application.

4a) Of the above claim(s) *11-13,15-25,34 and 36-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,26-33 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 August 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The request filed by fax on June 6, 2003 (Paper No. 19) for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/560803 is acceptable and a RCE has been established. Applicants requested that the RCE filed on June 5, 2003 via express mail (Paper No. 20) be disregarded. Claims 1-13, 15-39 are pending and claims 1-10, 14, 25-3 and 35 are currently under prosecution. An action on the RCE follows.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

The Office acknowledges the receipt of the corrected drawings received August 12, 2002 (Paper No. 11). The drawing have been reviewed and approved by the Draftsperson.

The rejection of claims 1-10, 14, 26-33 and 35 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of applicant's amendment.

The rejection of claims 1, 2, 9, 26, 27 and 34 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of applicant's amendment.

The rejection of claims 1, 9, 10 and 14, it is not clear if Markush claim format was intended in claims 10 and 14 **is withdrawn** in view of applicant's amendment.

The rejection of claim 1 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of applicant's amendments to the claims.

New rejection in view of applicants amendment's to the claims:

Claim Rejections - 35 USC § 112

The rejection of claim 1-10, 26-33 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. There are several components which are not clear in either the base claim or the dependent claim to list a few:

Claim 1, uses the term "selection marker" and "selection agent", it is not clear if the "selection agent" an antibiotic (claim 10 or claim 32) or 5-AZA-C (claim 33).

Claim 2 and 27, it is not clear what is intended with "selecting helper virus which is functional" does this mean antibiotic selection or is another selection intended?

Claim 28, it is not clear what is intended with "removing from a population of vector packaging cells..." does this mean antibiotic selection or is another removal intended?

Claim 29, it is not clear what is intended with "removing cell with inactivated virus by positive selection" does this mean antibiotic selection or is another selection intended?

Claim 33, it is not clear if antibiotic selection in addition to treatment of cells with 5-AZA-C is intended or does this treatment alone select for "functional helper virus".

The instant claims, specifically claim 1 and 26, are indefinite in the recitation of "a method for establishing a vector packaging cells" or "method of increasing the presence of viral titer" because the endpoint(s) of claimed methods are ambiguous and unclear. There is an absence or lack of clarity as to critical or resolutions steps or endpoints which reads back on the preamble of the claimed methods. In this instance the preamble indicates that the method establishes a vector packaging cell line, while the resolution step results in the production of viral particles not a packaging cell. Clarification so that the resolution step reads back on the preamble is required.

Claims 10 and 32 contains the trademark/trade name Zeocin™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a special formulation containing Phleomycin D1 and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

Claims 1-4, 6-9, 26-31 and 35 are rejected under 35 U.S.C. 102(e) being anticipated by Beach et al. (U.S Pat. No. 6,025,192) or (U.S. Pat. No. 6,255,071).

The instant invention is now drawn to a method of establishing a vector packing cells, by introducing a helper virus into the cell population. The term "helper virus" is interpreted to be (specification page 8 lines 14-30):

> A plasmid that enables positive selection of cells with active helper virus. More particularly an internal ribosome entry site along with a marker selection gene downstream of the *gag*, *pol*, and *env* genes provided positive selection of helper virus which had not been inactivated by methylation. "Helper virus" shall include any packaging deficient vector or nucleotide sequence encoding a viral protein, the expression of which is necessary in a vector producing cell for assembly an packaging of a particular vector capsid.

A viral vector containing a gene of interest is added to the cell containing the helper virus. The term "viral vector" is interpreted to be (specification page 9 lines 18-31):

> Viral vector shall include any viral based vector which embodies less than all structural proteins necessary for viral capsid assembly, and any additional nucleotide sequences desirable for expression or to be delivered to; a host cell. The instant invention utilizes the term "comprising" which can include more additional steps additional steps.

The selection of non-methylated helper virus is achieved by providing the selection pressure with an antibiotic (claims 1-4, 26, 27, 29, 30 and 35). The presence of an LTR linked to a viral production gene is sufficient to be capable of being methylated.

Beach et al. disclose the production of a retroviral vector packaging cell line (see section 5.6, U.S Pat. No. 6,025,192, columns 9-11 or U.S. Pat. No. 6,255,071, columns 17-21). The reference indicates the use of a polycistronic packaging cassette comprising at least two genes sequences important for efficient packaging of retroviral derived nucleic acid into functional

retroviral particles in operative association with a selectable marker and a quantifiable marker. The polycistronic expression cassettes allows for the selection of the selectable marker which ensures that only those cells expressing the gene sequence important for packaging are selected. The retroviral packaging cell lines of the reference optimize expression from retroviral LTR promoters (capable of being methylated). The packing cell lines can be developed which express gag, pol and or env proteins modified in a manner that promotes an increased viral titer an/or infectivity range (see also section 13.2-13.5, U.S Pat. No. 6,025,192, columns 35-38 or U.S. Pat. No. 6,255,071, columns 45-47). The reference disclose the production of a packing cell that provides gag, pol and/or env sequences which are then linked to an IRES linked to a selection maker in this case hygromycin (see figure 18 of U.S. Pat. No. 6,255,071). The reference also discloses a viral vector comprising a packing sequence containing a polylinker cloning site and an IRES with a selection marker (see figure 1 of , U.S Pat. No. 6,025,192, columns 35-38 or U.S. Pat. No. 6,255,071). Therefore, the instant invention is anticipated by Beach et al.

Claim Rejections - 35 USC § 103

Claims 1-10, 26-31 and 35 are rejected under 35 U.S.C. 103(a) being obvious Beach et al. (U.S Pat. No. 6,025,192) or (U.S. Pat. No. 6,255,071).

The instant invention is now drawn to a method of establishing a vector packing cells, by introducing a helper virus into the cell population. The term "helper virus" is interpreted to be (specification page 8 lines 14-30):

> A plasmid that enables positive selection of cells with active helper virus. More particularly an internal ribosome entry site along with a marker selection gene

> downstream of the *gag*, *pol*, and *env* genes provided positive selection of helper virus which had not been inactivated by methylation. "Helper virus" shall include any packaging deficient vector or nucleotide sequence encoding a viral protein, the expression of which is necessary in a vector producing cell for assembly an packaging of a particular vector capsid.

A viral vector containing a gene of interest is added to the cell containing the helper virus. The term "viral vector" is interpreted to be (specification page 9 lines 18-31):

> Viral vector shall include any viral based vector which embodies less than all structural proteins necessary for viral capsid assembly, and any additional nucleotide sequences desirable for expression or to be delivered to; a host cell. The instant invention utilizes the term "comprising" which can include more additional steps additional steps.

The selection of non-methylated helper virus is achieved by providing the selection pressure with an antibiotic (claims 1-4, 26, 27, 29, 30 and 35). The presence of an LTR linked to a viral production gene is sufficient to be capable of being methylated.

Beach et al. teach the production of a retroviral vector packaging cell line (see section 5.6, U.S Pat. No. 6,025,192, columns 9-11 or U.S. Pat. No. 6,255,071, columns 17-21). The reference indicates the use of a polycistronic packaging cassette comprising at least two genes sequences important for efficient packaging of retroviral derived nucleic acid into functional retroviral particles in operative association with a selectable marker and a quantifiable marker. The polycistronic expression cassettes allows for the selection of the selectable marker which ensures that only those cells expressing the gene sequence important for packaging are selected. The novel retroviral packaging cell lines of the invention optimize expression from retroviral LTR promoters (capable of being methylated). The packing cell lines can be developed which express gag, pol and or env proteins modified in a manner that promotes an increased viral titer an/or infectivity range (see also section 13.2-13.5, U.S Pat. No. 6,025,192, columns 35-38 or U.S. Pat. No. 6,255,071, columns 45-47). The reference disclose the production of a packing cell

that provides gag, pol and/or env sequences which are then linked to an IRES linked to a selection maker in this case hygromycin (see figure 18 of U.S. Pat. No. 6,255,071). The reference also discloses a viral vector comprising a packing sequence containing a polylinker cloning site and an IRES with a selection marker (see figure 1 of , U.S Pat. No. 6,025,192, columns 35-38 or U.S. Pat. No. 6,255,071).

The reference does not teach using the Ziocin as the selection marker in the helper virus construct. It would have been *prima facie* obvious to utilize any known mammalian antibiotic resistance marker that is functional in a mammalian cell as suggested by Beach et al. (see U.S Pat. No. 6,025,192, column 4, lines4-9). Zeocin (a.k.a. Pleomycin) resistance gene is a well-known and characterized protein in the art, it is known to be is non-toxic in a wide variety of cells and is a known antibiotic used for selection in mammalian cell culture. The advantage of using Zeocin is that the same antibiotic can be used in a bacterial culture and a mammalian cell culture. Beach et al. provides the motivation by suggest the use of any antibiotic which can function as a mammalian marker. Therefore, the instant invention is obvious over Beach et al.

Conclusion

Claims 1-10, 14, 26-33 and 35 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 or for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER 8/25/03